Office Action Summary	Application No.	Applicant(s)	
	10/611,593	LESAICHERRE ET AL.	
	Examiner	Art Unit	
	Nelson Yang	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 6-20* is/are pending in the application.

4a) Of the above claim(s) *17-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 6-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 June 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Claims 1-4, 6-16 are currently under examination.

2. Claims 17-20 are withdrawn.

Rejections Withdrawn

3. Applicant's arguments, see p. 2-5, filed January 5, 2009, with respect to the rejection of claims 1-3, 9, and 10 under 35 U.S.C. 103(a) as being unpatentable over Nock et al. [US 2002/0049152] in view of Eaton et al. [Eaton et al., S-Thiolation of HSP27 regulates its multimeric aggregate size independently of phosphorylation. 2002, 277(24): pp.21189-21196] have been fully considered and are persuasive. The rejection of claims 1-3, 9, and 10 under 35 U.S.C. 103(a) as being unpatentable over Nock et al. [US 2002/0049152] in view of Eaton et al. [Eaton et al., S-Thiolation of HSP27 regulates its multimeric aggregate size independently of phosphorylation. 2002, 277(24): pp.21189-21196] has been withdrawn.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-3, 9, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tolbert et al. [Tolbert et al., Intein-mediated synthesis of proteins containing carbohydrates and

other molecular probes, 2000 J Am Chem Soc, 122 (23): pp. 5421-5428] in view of Nock et al. [US 2002/0049152].

With respect to claims 1, 9, Tolbert et al. teach fusion proteins comprising N-terminal intein fusion proteins ligated to maltose binding proteins (p.5423, col.2), wherein the intein is mutated to only undergo the first step of protein splicing, intein-catalyzed thioester formation (p.5422, col.2, para. 2). Tolbert et al. specifically teach isolating MBP-intein fusion protein on a chitin column for purification, cleaving the MBP-intein fusion protein under conditions in which cysteine-thioester ligation takes place (p.5423, col.2) and the cleaved MBP was eluted off (p. 5424, col.1). Tolbert et al. further teach that the cysteine may be a biotinylated cysteine, wherein the biotin is attached to the C-terminal of the cysteine by an ethylenediamine linker which forms a peptide bond with the C-terminus of the cysteine (p.5423, col. 1 and fig. 2 (5)). Tolbert et al. teach that these cysteine derivatives mad be used to modify the C-terminus of proteins expressed as N-terminal intein fusions(p. 5423, col.2). Tolbert et al. do not specifically teach immobilizing the resulting biotinylated proteins to a support.

Nock et al., however, teach a method of immobilizing a polypeptide to a surface with mutant inteins where only the amino-terminal end of the intein participates in the reaction to form a thioester or ester bond (para. 0045, 0056, 0059) and a cysteine, serine or threonine (para. 0057), wherein the amino-terminal end of the intein is capable of splicing of the N-extein of the cysteine, serine, or threonine to the C-extein, forming thioesters with an activating compound at the end of the extein (para. 0057-0059). Specifically, Nock et al. teach expressing a chimeric gene that encodes a fusion protein which comprises a polypeptide and an intein (para. 0013), attaching anchor molecules comprising cysteine to the polypeptides by a thioester linkage and

anchoring the polypeptides to a surface (para. 0014, 0056). Nock et al. also teach that tags may be used to attach the polypeptides to the surface to form arrays or for purification of the polypeptides (para. 0065), and that this allows for the construction of polypeptide arrays wherein the polypeptides are generally in the same orientation, can be full-length, biologically active, and readily screened for a desired activity (abstract, para. 0047).

One of ordinary skill in the art at the time of the invention, in view of the combination of Nock et al. and Tolbert et al. would have had a reasonable expectation of success in immobilizing the resulting biotinylated proteins of Tolbert et al. to a support, by using the biotin group of the protein to bind to an avidin group on the support.

Therefore, one of ordinary skill in the art at the time of the invention would have been motivated to use a biotinylated cysteine to splice the fusion protein of Nock et al., as suggested by Tolbert et al., and immobilize the resulting protein onto a support using the biotin group of the protein to bind to a avidin group on the support, as this would allow the construction of polypeptide arrays wherein the polypeptides are generally in the same orientation, can be full-length, biologically active, and readily screened for a desired activity.

6. With respect to claims 2, 10, Nock et al. teach that tags may be used to attach the polypeptides to the surface to form arrays or for purification of the polypeptides (para. 0065), wherein the tags may be avidin (claim 12), which would bind to the biotinylated proteins.

7. With respect to claim 3, Nock et al. the substrate of the array may be glass (para. 0119).

8. Claims 4, 11-16 are rejected under 35 U.S.C. 103(a) as being unpatentable Tolbert et al. [Tolbert et al., Intein-mediated synthesis of proteins containing carbohydrates and other

molecular probes, 2000 J Am Chem Soc, 122 (23): pp. 5421-5428] in view of Nock et al. [US 2002/0049152], as applied to claims 1, 9 above, and further in view of Duan [US 6,951,742].

With respect to claims 4, 11, Tolbert et al. and Nock et al. teach the invention as discussed above, but fail to teach that the proteins are expressed by a pTYB1 expression vector.

Duan, however, teaches the use of pTYB1 vectors to express fusion proteins, and further teach that pTYB1 vectors allow the cloning of a target gene immediately adjacent to the intein cleavage site, which results in the purification of a native target protein without any vector derived extra residues after the cleavage (column 32, lines 52-65).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to use a pTYB1 expression vector to express the fusion proteins of Tolbert et al. and Nock et al., as suggested by Duan, in order to allow the cloning of a target gene immediately adjacent to the intein cleavage site, allowing for the purification of a native target protein without any vector derived extra residues after the cleavage.

9. With respect to claim 12, Tolbert et al. teach isolating the fusion protein on a chitin column (p. 5423, col.2).

10. With respect to claim 13, Tolbert et al. teach that the cysteine derivatives such as cysteine-biotin is added to the chitin column (p. 5423, col.1-2).

11. With respect to claim 14, Nock et al. teach substrates comprising glass (para. 0119).

12. With respect to claim 15, Nock et al. teach streptavidin (claim 12).

13. With respect to claim 16, Duan teaches spotting the protein onto a solid surface to form an array (column 37, lines 1-25).

14. Claims 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tolbert et al. [Tolbert et al., Intein-mediated synthesis of proteins containing carbohydrates and other molecular probes, 2000 J Am Chem Soc, 122 (23): pp. 5421-5428] in view of Nock et al. [US 2002/0049152], as applied to claim 2 above, and further in view of Bradley et al. [US 2002/0006623].

With respect to claims 6, 7, Tolbert et al. and Nock et al. teach the invention as discussed above, but fail to teach that the glass support is derivatized with an epoxy silane compound such as glycidoxypropyl trimethoxysilane.

Bradley et al., however, teach the dervizatization of glass supports with glycidoxypropyl trimethoxysilane (para. 0127), and further teach that glycidoxypropyl trimethoxysilane is rapid, and occurs under very mild conditions using a minimum of inexpensive reagents (para. 0128).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to have derivatized the glass supports of Tolbert et al. and Nock et al. with glycidoxypropyl trimethoxysilane, as suggested by Bradley et al., in order to be able to attach ligands to the glass support rapidly, and under very mild conditions while using a minimum of inexpensive reagents, which would render it cheaper, quicker, and simpler that other methods.

15. With respect to claim 8, Nock et al. teach streptavidin (claim 12).

Response to Arguments

16. Applicant's arguments with respect to claims 1-4, 6-16 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

17. No claims are allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nelson Yang whose telephone number is (571)272-0826. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on (571)272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

19. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nelson Yang/
Patent Examiner, Art Unit 1641